Pharmacovigilance information for pharmaceutical companies

Electronic transmission of individual case safety reports (ICSRs) with ANSM
(French National Agency for the safety of Medicines and Health Products)

This document supersedes that published in October 2008, updated in June 2009 and July 2012

Last update: November 2017

A French version of this document is available

OUTLINE

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   o Non-serious

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INTRODUCTION

This document:

- **concerns electronic transmission of ICSRs** possibly related to medicines and products as listed in articles L 5121-1 and R. 5121-150 of the French Public Health Code and received by exploitant pharmaceutical companies. These ICSRs can be spontaneous or solicited reports transmitted by healthcare professionals, patients or other reporters, or post authorisation study reports.
- **does not concern** the transmission of suspected unexpected serious adverse reactions (SUSARs) occurring in the context of interventional clinical trials.

This document is updated as part of:

- implementation of a new version of EudraVigilance by the EMA, integrating new functionalities from 22 November 2017, further to the change in European pharmacovigilance legislation, especially concerning the electronic transmission of individual case safety reports (ICSRs) between the various stakeholders, in order to:
  - streamline information exchange,
  - ensure more effective monitoring of the safety of use of medicinal products,
  - enrich the content of the exchanged data.

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### A) TRANSMISSION OF INDIVIDUAL CASE SAFETY REPORTS FOR ADVERSE EFFECTS OCCURRING IN FRANCE OR IN THE EUROPEAN UNION

#### SERIOUS

<table>
<thead>
<tr>
<th>Marketing Authorisation procedure</th>
<th>Country of occurrence</th>
<th>Severity type and time to reporting</th>
<th>Transmission from 22 November 2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Centralised</td>
<td>France or European Union</td>
<td>Serious (15 days)</td>
<td>EudraVigilance</td>
</tr>
<tr>
<td>• Mutual recognition decentralised,</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>• National</td>
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<td></td>
</tr>
</tbody>
</table>

NB: for pharmaceutical companies already reporting to EudraVigilance → this method of transmission should continue to be used.

#### NON-SERIOUS

<table>
<thead>
<tr>
<th>Authorisation/registration procedure</th>
<th>Country of occurrence</th>
<th>Severity type and time to reporting</th>
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<td>France or European Union</td>
<td>Non-serious (90 days)</td>
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<td>• Mutual recognition decentralised,</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>• National</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
B) TRANSMISSION OF INDIVIDUAL CASE SAFETY REPORTS FOR ADVERSE EFFECTS OCCURRING OUTSIDE THE EUROPEAN UNION

**SERIOUS**

<table>
<thead>
<tr>
<th>Authorisation/registration procedure</th>
<th>Country of occurrence</th>
<th>Severity type and time to reporting</th>
<th>Transmission from 22 November 2017</th>
</tr>
</thead>
<tbody>
<tr>
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<td>Outside European Union</td>
<td>Serious (15 days)</td>
<td>EudraVigilance</td>
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<td>• Mutual recognition decentralised,</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• National</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**NON-SERIOUS**


C) OTHER INFORMATION

1/ New procedures for the exchange of ICSRs between the ANSM and marketing authorisation holders (MAH)

Individual case safety reports notified to the ANSM via the network of Regional Pharmacovigilance Centres are transmitted electronically by the ANSM to the EMA since 20 November 2005 (via Eudravigilance). For information, the individual case safety reports will be sent by post to the operator(s) of the medicinal products concerned (coded to be suspect or in interaction) until 21 November 2017. From 22 November 2017, the ANSM shall no longer send individual case safety reports of serious adverse effects to pharmaceutical companies by post. They should use the EudraVigilance EVWEB functionalities directly to access and download the serious and non-serious ICSRs by which they are concerned. ICSRs originating from ANSM are mainly in French and it will be transmitted as it to Eudravigilance. They will be accessible from 22 November 2017 after Eudravigilance downtime.

Concerning individual case safety reports from medical and scientific literature, pharmaceutical companies are no longer required to forward the corresponding articles to the ANSM since 10 July 2017.
2/ New international standards

Pharmaceutical companies should finalise processes and their IT infrastructures to bring them into compliance with the new international ICH E2B (R3) standards by 22 November 2017. The document describing the technical changes is available in the ‘Eudravigilance stakeholder change management plan’ issued by the EMA. It can be downloaded at:

3/ EudraVigilance data monitoring

From 22 November 2017, MAH will have extended access to EudraVigilance data to enable them to continuously monitor the information in this database in the aim of detecting pharmacovigilance signals (see Commission Implementing Regulation (EU) 520/2012 of 19 June 2012 on the performance of pharmacovigilance activities).

The new provisions shall be implemented gradually:

- One-year pilot phase, during which MAH should monitor the data for active substances on the list of medicinal products under additional monitoring, due to come into effect from 22 November 2017,
- Implementation of the pilot phase from 22 February 2018: MAH should monitor the data in EudraVigilance for active substances on the list of medicinal products under additional monitoring, and inform the EMA and the competent authorities if they detect ‘confirmed signals’ among the data,
- For the other substances not on the list of medicinal products under additional monitoring, MAH will have access to EudraVigilance that they can use as additional data source for their signal detection activities. However, they are not required to continuously monitor EudraVigilance for these substances.
- Between 22 November 2017 and 22 February 2018, MAH are required to familiarise themselves with the tools developed in order to enable monitoring of EudraVigilance data.

Additional information and training can be found on the EMA website:
http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000162.jsp &mid=WC0b01ac0580a1a1fb

For information relating to data exchange with Eudravigilance, please contact the EMA: EMA IT Service Desk, Tel. +44 (0)20 3660 7523
For specific information to France, please send an email to: anpv@ansm.sante.fr
APPENDIX 1

TECHNICAL SPECIFICATIONS FOR REPORTING TO EUDRAVIGILANCE

The EV-PM module is used for electronic reporting to EudraVigilance. Accordingly, the receiver's ID of the ICSRs must be: EVHUMAN.

The various steps for registering with the EudraVigilance production environment are described on the Eudravigilance website at: http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000687.jsp&mid=WC0b01ac0580a69262

MedDRA

The MedDRA terms used should derive from the latest published version of the terminology. Low level terms (LLT) should be ‘common’ in this latest version. The notion of latest published version should comply with MSSO (MedDRA Maintenance and Support Services Organization) and EMA EudraVigilance Expert Working Group recommendations.

Languages

The languages accepted by ANSM for electronic ICSRs are French and English.

Imputability

For ICSRs occurring in France, the drug causality assessment according to the French imputability method should be included in the ICSRs in section B.4.k.18 (Relatedness of drug to reaction(s)/event(s)) for E2B(R2) message or G.k.9.i.2.r (Assessment of relatedness of drug to reaction(s)/event(s)) for E2B(R3) message.

The method used ((B.4.k.18.3 for E2B(R2) or G.k.9.i.2.r.2 for ICH E2B(R3)) should be worded 'FRENCH IMPUTABILITY METHOD' and the result (B.4.k.18.4 for ICH E2B(R2) or G.k.9.i.2.r.3 for ICH E2B(R3)) provided in the format ‘CxSyBz’ (x, y and z representing the chronological, semiological and bibliographical imputability scores respectively).
APPENDIX 2
REMINDER OF THE CONSEQUENCES FURTHER TO CHANGE OF NAME OF THE AGENCY
FROM THE AFFSAPS TO THE ANSM

FR-AFSSAPS-yyyyyy identifiers should not be migrated to FR-ANSM-yyyyyy identifiers.

In order to maintain consistency between all of the pharmacovigilance databases, and until further notice:

2.1. The REPORTDUPLICATE section (A.1.11) from E2B(R2) message or Source(s) of the Case Identifier(s) (C.1.9.1.r) from ICH E2B(R3) message should be filled in as follows:

<table>
<thead>
<tr>
<th>E2B(R2)</th>
<th>A.1.11.1</th>
<th>DuplicateSource</th>
<th>ANSM</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>A.1.11.2</td>
<td>DuplicateNumb</td>
<td>ANSM</td>
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<tr>
<td>E2B(R3)</td>
<td>C.1.9.1.r.1</td>
<td>Source(s) of the Case Identifier</td>
<td>ANSM</td>
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<tr>
<td></td>
<td>C.1.9.1.r.2</td>
<td>Case Identifier(s)</td>
<td>Keep the FR-AFSSAPS-yyyyyy number</td>
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</tbody>
</table>

2.2. The LINKEDREPORT section (A.1.12) from E2B(R2) message or Identification Number of the Report Which Is Linked to This Report (C.1.10.r) from E2B(R3) message should be filled in as follows:

<table>
<thead>
<tr>
<th>E2B(R2)</th>
<th>A.1.12</th>
<th>LinkReportNumb</th>
<th>Keep the FR-AFSSAPS-yyyyyy number</th>
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<tbody>
<tr>
<td>E2B(R3)</td>
<td>C.1.10.r</td>
<td>Identification Number of the Report Which Is Linked to This Report</td>
<td>Keep the FR-AFSSAPS-yyyyyy number</td>
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